

Original Research Article

Profile and outcomes of referred neonates needing immediate resuscitation at admission

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ABSTRACT

Background: Referral of sick newborns to a tertiary centre for management is common. Deterioration in the baby's condition can occur during transport and affects the outcome of babies. Many babies reach the referral centre in an unstable condition and need resuscitation immediately on arrival in the emergency. We aimed to study the profile and outcomes of such babies.

Methods: This prospective observational study over a period of 8 months aimed at understanding the profile and demographic characters of neonates needing immediate resuscitation at admission and analysing their outcomes. We included all neonates who were resuscitated at admission and followed their hospital course until discharge or death.

Results: A total of 133 (21%) of all the referred babies who fulfilled the inclusion criteria were enrolled. Most of the babies were male, born at term and were less than 24 h old. Ambulances were the mode of transport for 117 (88%) babies. Mortality was seen in 68 (51.1%) babies with 36 (52.9%) deaths occurring within 24 hours of admission. Need for inotropes at admission was strongly associated with mortality, the relative risk being 5.30 with a confidence interval of (2.3, 12). Age < 48 hours and distance travelled > 15 km were also associated with high risk of mortality.

Conclusions: Neonates needing immediate resuscitation at admission have high rates of mortality. Factors like shock at admission, distance travelled, and age of the baby should be considered and taken into account before a baby is referred to another centre for management. Risk factors associated with poor outcomes should be considered and managed before and during transport.

Keywords: Emergency department, Inotropes, Mortality, Newborn, Shock

INTRODUCTION

Neonatal morbidity and mortality continue to be raging global public health problems. A recent publication by UNICEF reported over 2.4 million newborn deaths worldwide in the year 2020.^{1,2} Majority of the burden is borne by the lower-middle-income countries (LMICs) of Asia and Africa. The Southeast Asian countries have extremely high neonatal mortality rates (NMR) ranging from 1-30/1000 live births.³ Neonatal mortality is very high in our country (24.4/1000 live births) and even

higher in the state of Uttar Pradesh (35/1000 live births).⁴ Multiple factors are responsible for such poor neonatal health statistics; poverty, undernutrition, poor health of the mother, low literacy and less spacing between pregnancies being important factors which start playing a role even before conception.⁵ Factors that are important after conception are, irregular antenatal checkups, poor availability of quality health care, lack of nutrition and adequate rest, failure to take supplements etc.⁶ Factors after the birth of the baby are improper care at and after birth, failure to initiate breastfeeding within one hour of

birth, high prevalence of top feeding, unhealthy rearing practices, poor hygiene and delay in seeking health care.⁷

Scarcity of specialized care for newborns in most health facilities make referrals of sick neonates to higher centre inevitable. In-utero transport of newborns is the best and safest means of referral but may not be feasible in many cases.⁸ Deterioration in baby's condition is common during transport and ultimately contributes to poor prognosis. Neonatal transport is challenging, even developed nations are facing challenges in standardization and optimizing neonatal transport practices.⁹

Ill equipped health facilities both in government and private sectors, high birth rate, poorly motivated and untrained health care workers, shortage of manpower and high cost of private healthcare add to the burden of more newborns being referred for intensive care.⁷

This ultimately results in a baby who reaches the referral center in an unstable state. Some neonates may unfortunately die enroute before reaching the referral center and are declared "brought dead (BD)" in the emergency department, if revival despite all possible efforts is not successful. Large numbers of such BD neonates are brought to tertiary care hospitals in LMICs.^{10,11} Majority of BD cases brought to an emergency department of tertiary care hospitals are newborns.¹² Such brought dead babies are not accounted for in any morbidity and mortality statistics.

Many authors in the past have studied referral patterns, admission characteristics and outcomes of referred babies.^{8,11,13} These studies emphasize the overall characters of referred babies. We wanted to highlight only those babies who were very unstable at admission and needed immediate resuscitation. To the best of our knowledge, none of the authors have specifically studied neonates needing resuscitation at admission in the emergency department. We conducted a study to look at the profile and outcomes of such neonates.

METHODS

This was a prospective cohort study conducted in the emergency department and the neonatal intensive care unit (NICU) of a tertiary level teaching institute. Ours is a 20 bedded, level III extramural NICU and is a referral centre for adjoining areas. The study was done from April 2023 to November 2023 over a period of 8 m. The study was approved by the Institutional Ethics committee (IEC). Informed consent was taken from one of the parents after initial management of the baby.

All neonates (<28 d) needing immediate resuscitation at presentation to the emergency department were included in the study. Babies who were declared "brought dead" after resuscitative attempts were excluded from the study.

All neonates at presentation were kept under a servo-controlled radiant warmer and emergency management was done as per protocols. A saturation monitoring probe was immediately put in place. Babies who were gasping or apneic were given positive pressure ventilation by a self-inflating bag and mask and then intubated by an appropriate size endotracheal tube (ETT). Babies who arrived with ETT *in situ* were started on bag and tube ventilation. If the ETT was found to be displaced, another tube was inserted and bag and tube ventilation initiated. Blood sugar was checked using a glucose strip on arrival and intravenous access was obtained. A thorough and complete examination of the baby was then done. The NICU team was informed to prepare a bed and make all necessary arrangements for shifting the baby to the NICU. Investigations were sent for each baby as per their needs. Other emergency management like administration of dextrose or saline bolus, inotropes, anticonvulsants etc. was done as per the baby's requirements. Another doctor then took the detailed history regarding demographic details, and the relevant medical aspects reviewed the documents of previous admission, if any, and the documents related to the mother's antenatal course and birth of the baby. After overall assessment of the baby, the parents were counselled regarding the condition of the baby, the prognosis and the further plan of action.

Hypoglycemia was defined as blood sugar level <45 mg/dL. Hyperglycemia was defined as blood sugar level >125 mg/dl. Hypothermia was defined as axillary temperature <36.5°C, mild (36-36.4°C), moderate (32-35.9°C) and severe (<32°C). Fluid refractory shock was defined as shock not responding to two boluses of normal saline at 10 ml/kg over 10-15 min. Such babies were started on inotropic support. Choice of inotrope depended on the clinical diagnosis of the baby.

The baby was then shifted to the NICU in a transport incubator and further management was done according to the baby's condition as per standard protocols. The hospital course was followed up till discharge or death.

Statistical analysis

The statistical analysis was done using Epi info 7.2.6.0 software. The numerical values were expressed as mean and standard deviation (SD) for normally distributed data and median and interquartile range (IQR) for non-normally distributed data. Qualitative data were represented as proportions and percentages. Student's t test was applied to compare numerical data and chi square was used to compare qualitative data. Multiple logistic regression analysis was performed to study the effect of various factors on risk of mortality. A p value of less than 0.05 was considered significant.

RESULTS

A total of 632 babies were referred to the NICU in the 8 m of study period. Out of these, 133 (21%) babies needed

immediate resuscitation at presentation to the emergency department and were included in the study. Most babies were male and born at term gestation (Table 1). Babies travelled long distances from the place of delivery; the maximum distance travelled was 347 km. The travel time varied from 15 minutes to more than 6 hours. Sixty-five (65) babies travelled more than 15 km to reach our hospital. Babies brought by an ambulance were 117 (88%), and 39 (29.3%) babies had an ETT *in situ*. Perinatal asphyxia (PA) was the primary diagnosis at admission in 65 (49%) babies.

Fluid refractory shock was seen in 54 (40.6%) babies who were started on inotropic support (Table 2). Mortality was seen in 68 (51.1%) babies with 36 (52.9%) deaths occurring within 24 hours of admission.

We found there was no significant difference in the birth weight, (Table 3) gestational age (GA), distance travelled, blood sugar at admission and duration of ventilation between babies who died or were discharged.

On multivariate logistic regression, the need for inotropes at admission was strongly associated with mortality, the relative risk (RR) of 5.30 with a confidence interval (CI) of (2.3, 12) and a $p < 0.001$. Age of referral < 48 hours and travel of more than 15 km was also significantly associated with mortality. (Table 4).

Table 1: Demographic characteristics of the study population, (n=133).

Characteristics	N
Birth weight (mean [SD]) (kg)	2.3 (0.7)
Gestational age (mean [SD]) (weeks)	36.01 (3.4)
Preterm babies	54 (40.6)
Sex (M:F)	2:1
Vaginal deliveries	85 (63.9)
Age at admission (median [IQR]) (days)	1 (0.3)
Babies admitted on day 1 of life	68 (51.1)
Distance travelled (median [IQR]) (km)	7 (4,16), Max=357
Referred from	
Govt hospital	53 (39.8)
Private hospital	65 (48.8)
Brought from home	15 (11.4)
Mode of transport	
Ambulance	
Supplemental oxygen	72 (54.1)
ETT and bag ventilation	36 (27)
Ventilator	7 (5.3)
Without oxygen	2 (1.5)
Bike	11 (8.4)
Car	4 (3)
Bus	1 (0.7)

Table 2: Clinical characteristics of the babies at admission.

Characteristics	N (%)
Hyperglycemia	59 (44.3)
Hypoglycemia	10 (7.5)
Hypothermia	61 (45.8)
Mild	50 (37.5)
Moderate	11 (8.4)
Need of inotropes at admission	54 (40.6)
Primary diagnosis	
Perinatal asphyxia	65 (48.9)
Prematurity/ low birth weight	27 (20.3)
Sepsis	21 (15.8)
Meconium aspiration syndrome	13 (9.8)
Congenital malformation	4 (3)
Others	3 (2.2)
Outcome	
Discharge	65 (48.9)
Death	68 (51.1)
Death < 24 hrs of admission	36 (52.9)

Table 3: Comparison of characteristics between babies who died or were discharged.

Characteristics	Death	Discharged	P value
Distance travelled (km)*	6.5 (4,13.5)	8 (4,18)	0.10
Birth weight (kg)#	2290 (680)	2150 (760)	0.28
BS at admission (mg/dl)#	120.5 (45)	124.5 (68)	0.7
Duration of stay (d)*	2 (1,5)	14 (8,19)	< 0.001
Duration of ventilation (d)*	2 (2,5)	3 (1,5)	0.19

*Median (interquartile range), #Mean (SD), BS blood sugar

Table 4: Multivariate logistic regression for risk of mortality.

Characteristics	Unadjusted RR (CI)	P value
Male sex	1.2 (0.8, 1.7)	0.27
Birth wt < 1500 g	1.2 (0.8, 1.7)	0.26
Vaginal delivery	0.75 (0.5, 1)	0.1
Distance travelled > 15 km	1.36 (1.1, 1.8)	0.047*
Admission age < 48 h	2.11 (1.01, 4.37)	0.04*
Prematurity	0.77 (0.5, 1.1)	0.14
Perinatal asphyxia	1.07 (0.76, 1.5)	0.67
MAS	1.2 (0.6, 2.4)	0.64
Hyperglycemia	1.44 (0.66, 3.12)	0.34
Need of inotropes	5.30 (2.34, 12.01)	< 0.001 *
Hypothermia	0.75 (0.35, 1.6)	0.47

*Significant, RR-relative risk, CI-confidence interval, MAS-meconium aspiration syndrome.

DISCUSSION

We studied 133 babies who needed immediate resuscitation at admission. These babies constituted 21% of the total referrals during the study duration. Most of the babies were male, born at term were less than 24 h old. Ambulances were the mode of transport for most babies. Hyperglycemia was common at admission; seen in 44% of babies. Need for inotropes at admission, age <48 hours and distance travelled >15 km were associated with high risk of mortality.

Health seeking behaviour has gender bias. A male baby is more likely to be taken to a referral health facility for treatment than a female baby. Cavallin et al in its study on neonatal transport reported males to constitute around 57% of all the referred babies.¹⁴ Male preponderance is seen in all other studies on neonates being referred for admission.¹³ In our study they constituted almost two thirds of the study population which is higher than other studies.

A rise in proportion of caesarean section deliveries is being seen globally, including India. In the public hospitals, vaginal delivery rates are much higher than in the private sector. Cavallin et al had a high rate of vaginal deliveries (98.5%) in their study, so is the case in other studies.^{13,14} We had lower percentage of vaginal deliveries (64%). The high incidence of vaginal deliveries in the referred neonates could be because most babies were born in a public health facility. Also, most places that are equipped to conduct a Caesarean section may have their own NICUs and may need referral less frequently. That may not be true for health care facilities conducting vaginal deliveries.

The first 72 hours of birth are the most crucial for a newborn, when the transition from intrauterine to extrauterine life occurs. Birth related events and prematurity are the commonest cause of NICU admissions in the first three days of life. Majority newborns need to be referred within the first 24 h of life, which has been reported in earlier studies also.^{13,14} Fifty-one percent (51%) admissions were of babies within 24 hours of birth. Although 20% of total admitted babies in our unit are less than 24 hours old, more than 50% of those needing ventilation at admission were less than 24 hours old.

Almost 80% of deaths in neonates occur in the first week of life, out of which two-thirds (62%) occur within the first 3 days of life, two-thirds of these occur within 24 hours of birth.¹⁵ Ninety-eight percent (98%) deaths due to asphyxia, 83% due to prematurity, 47% due to sepsis and 78% due to malformations occurred in the first week of life.¹⁵

Different studies report variable distances travelled by neonates and their families to reach the referral centre. Most of the well-equipped NICUs are concentrated in big

cities. Newborns requiring intensive care may need to travel long distances, which may have adverse impact on their outcomes.^{11,16} In the study by Narang et al the time taken to reach the hospital was significantly associated with poor outcomes.¹⁷ The odds ratio (OR) for mortality for babies travelling for more than 6 hours was 81 ($p<0.01$). Babies travelling more than 15 km had poorer outcomes in terms of mortality in our study.

Many neonates reach the referral unit in a clinically unstable condition and may need cardio-pulmonary resuscitation at admission. Singh et al in their study reported that 10% of the referred neonates needed resuscitation at admission, 10.4% required endotracheal intubation and shock was seen in 19% of all the babies.¹³ Resuscitation at admission was associated with high mortality; 48.9% of babies who received resuscitation at admission expired and 52% of these mortalities occurred within 24 h of admission. Deaths occurred soon after arriving even before they could be shifted to the NICU in 46% babies. Presence of shock at admission was associated with high risk of mortality (OR 6.65; CI 3.7, 11.8). Intubation at admission had OR of 26.82 (CI; 10.15, 70.8) for mortality which was the highest amongst all the antenatal, natal, transport and admission factors. In a study by Kalyan et al, presence of shock had an OR of 4.76 (CI; 1.8,12.58).¹⁸ In our study of babies needing resuscitation at admission, 40% had fluid refractory shock which was strongly associated with high risk of mortality.

Neonates needing cardiopulmonary resuscitation (CPR) have very poor outcomes.¹⁹ Handley et al reported 65% mortality in babies admitted in NICU who needed CPR. Need for vasoactive agents was associated with high risk of death ($aOR=2.77$). The babies in this study were in a controlled environment where immediate intervention was possible. Babies needing CPR at admission fare even worse. Such babies may have been hypoxic or in shock for an undetermined time and hypothermia is usually associated, therefore the mortality is even higher.

Characteristics of the baby at arrival have been evaluated in many studies and an association has been found between these clinical characteristics and outcomes of admitted babies. The TOPS (temperature, oxygen saturation, pulse and sugar levels) score has been validated by many authors and researchers and found to be a good indicator of outcomes.^{20,21}

All babies in our study were hypoxic and needed positive pressure ventilation at arrival, although 86% babies were getting supplemental oxygen during the transport. Babies may become hypoxic even when they are given supplemental oxygen by nasal prongs as they may need higher flow of oxygen or continuous positive airway pressure (CPAP) or mechanical ventilation. Providing these during transport remains a challenge in most developing countries.

Most neonates become hypothermic when they reach the referral center, and this adversely affects their outcomes. All studies observed high incidences of hypothermia in neonates at admission; the incidence varies from 30-80%.^{13,16,22} We had 46% babies who had hypothermia at admission. Out of these hypothermic babies, majority had mild hypothermia (cold stress). Incidence of hypothermia may vary with the season and environmental temperature. We conducted the study from April to October which is mostly summer season with high ambient temperature and that may be a reason why majority of babies were not severely/moderately hypothermic at admission. Presence of mild hypothermia did not affect the outcomes in these babies.

Glucose disturbances are commonly seen in referred neonates and have also been associated with poor outcomes. Most studies on referred neonates document hypoglycemia to be common and associated with poor outcomes. Incidence of hypoglycemia at admission varied from 13-46% in different studies.^{20,23} With easy availability of intravenous fluids, majority of babies may not be hypoglycemic at admission. We had a much lower rate of hypoglycemia at admission which was 7.5%. We, on the contrary, observed a high incidence of hyperglycemia (44%) which has not been reported earlier. Hyperglycemia has been associated with poor outcomes in newborns.^{24,25} Mishra et al reported that 33.7% of the referred newborns in their study were hyperglycemic at the time of admission.²⁶ Hyperglycemia and its association with poor outcomes has not been studied in referred neonates earlier and needs further evidence.

The primary diagnosis of the referred babies was PA in 31.6% babies, prematurity/low birth weight in 20.3%, meconium aspiration syndrome (MAS) with PA 17.3%, MAS alone in 9.8%, and sepsis in 15.8%. Most of the studies show a similar pattern of referred neonates.^{14,22}

Mortality is significantly higher in referred (extramural) babies than inborn babies irrespective of the birth weight and GA.^{10,12,27-29} Previous studies have reported mortality rates of 10-54% among referred neonates. Mathur et al reported 100% mortality in babies who had hypothermia, hypoglycemia, poor saturation and delayed capillary refill time (CRT) (all present) at admission.³⁰ Of the babies who died, 41.7% had an abnormal heart rate at admission. Babies who were received in an unstable condition (abnormalities in temperature, respiratory rate and heart rate) had a very high mortality rate of 91.7%.¹¹ Ours is a unit admitting only extramural babies, and we studied only neonates brought intubated or needing resuscitation at admission, therefore mortality was high, which was consistent with other studies.

Limitation of our study is that this is a single centre study and therefore may lack generalizability. We did not study the details of resuscitation at admission, type and

management of shock, which can give a better insight about the medical condition of the baby at presentation.

CONCLUSION

Pre-transport stabilization and care of the newborn during transport is the most important factor which can improve outcomes in babies. Factors like shock at admission, distance travelled, and age of the baby should be considered and taken into account before a baby is referred to another centre for management. Quality improvement initiatives are needed in these aspects of neonatal referral. Future studies on pre-transport and during transport interventions to prevent hypoxia and shock should be conducted so as to improve the outcomes of neonates when they ultimately reach the referral centre.

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